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(alkanoyl adj5 $carnitine) same liposome	4

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US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L3

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Search History

DATE: Monday, December 19, 2005 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L3	(alkanoyl adj5 $carnitine) same liposome	4	L3
L2	(ester adj5 $carnitine) same liposome	9	L2
L1	ester adj5 $carnitine	167	L1

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Search Results - Record(s) 1 through 9 of 9 returned.

☐ 1. Document ID: US 6797281 B1

Using default format because multiple data bases are involved.

L2: Entry 1 of 9 File: USPT Sep 28, 2004

US-PAT-NO: 6797281
DOCUMENT-IDENTIFIER: US 6797281 B1
** See image for Certificate of Correction **

TITLE: Esters of I-carnitine or alkanoyl I-carnitines

DATE-ISSUED: September 28, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Pisano; Claudio	Aprilia			IT
Tinti; Maria Ornella	Rome			IT
Santaniello; Mose	Nettuno			IT
Critelli; Luciana	Pomezia			IT
Salvatori; Giovanni	Rome			IT

US-CL-CURRENT: 424/450; 424/43, 424/434, 424/449, 424/46, 514/506, 554/30

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 2. Document ID: US 6476243 B1

L2: Entry 2 of 9 File: USPT Nov 5, 2002

US-PAT-NO: 6476243
DOCUMENT-IDENTIFIER: US 6476243 B1

TITLE: Perfluorinated esters of alkanoyl L-carnitine for the preparation of cationic lipids for the intracellular delivery of pharmacologically active compounds

DATE-ISSUED: November 5, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Santaniello; Mose	Nettuno			IT
Critelli; Lucia	Pomezia			IT

Scafetta; Nazareno	Pavona di Albano	IT
Cima; Maria Grazia	Civitavecchia	IT
Tinti; Maria Ornella	Roma	IT
Pisano; Claudio	Aprilia	IT
Pucci; Andrea	Albano Laziale	IT

US-CL-CURRENT: 554/121; 554/123, 554/225, 554/231, 560/170, 560/172

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 3. Document ID: US 6274321 B1

L2: Entry 3 of 9 File: USPT Aug 14, 2001

US-PAT-NO: 6274321
DOCUMENT-IDENTIFIER: US 6274321 B1

TITLE: High throughput functional screening of cDNAs

DATE-ISSUED: August 14, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Blumberg; Bruce	Irvine	CA		

US-CL-CURRENT: 435/6; 435/91.1, 435/91.2, 536/24.3, 536/24.31, 536/24.32, 536/24.33, 536/25.3, 536/25.32

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 4. Document ID: US 6180355 B1

L2: Entry 4 of 9 File: USPT Jan 30, 2001

US-PAT-NO: 6180355
DOCUMENT-IDENTIFIER: US 6180355 B1
** See image for Certificate of Correction **

TITLE: Method for diagnosing and treating chronic pelvic pain syndrome

DATE-ISSUED: January 30, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Alexander; Richard B.	Ellicott City	MD		
Ponniah; Sathibalan	Ellicott City	MD		

US-CL-CURRENT: 435/7.1; 435/7.8

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 5. Document ID: US 5972600 A

L2: Entry 5 of 9 File: USPT Oct 26, 1999

US-PAT-NO: 5972600
DOCUMENT-IDENTIFIER: US 5972600 A

TITLE: Separation of active complexes

DATE-ISSUED: October 26, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Szoka, Jr.; Francis C.	San Francisco	CA		
Xu; Yuhong	San Francisco	CA		
Wang; Jinkang	San Francisco	CA		

US-CL-CURRENT: 435/6; 435/458, 977/DIG.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 6. Document ID: US 5876747 A

L2: Entry 6 of 9 File: USPT Mar 2, 1999

US-PAT-NO: 5876747
DOCUMENT-IDENTIFIER: US 5876747 A

TITLE: Liposome preferentially traveling to cardiac and skeletal muscles

DATE-ISSUED: March 2, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Stracher; Alfred	Roslyn Estates	NY	11576	
Kesner; Leo	Brooklyn	NY	11234	

US-CL-CURRENT: 424/450; 514/78, 514/821, 554/79, 554/80

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 7. Document ID: US 5008288 A

L2: Entry 7 of 9 File: USPT Apr 16, 1991

US-PAT-NO: 5008288
DOCUMENT-IDENTIFIER: US 5008288 A

TITLE: Carnitine directed pharmaceutical agents

DATE-ISSUED: April 16, 1991

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Stracher; Alfred	Roslyn Estates	NY	11576	
Kesner; Leo	Brooklyn	NY	11234	

US-CL-CURRENT: 514/535; 424/450, 428/402.2, 514/17, 514/2, 514/305, 514/547, 514/556, 514/821, 530/330, 530/812

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 8. Document ID: US 4866040 A

L2: Entry 8 of 9 File: USPT Sep 12, 1989

US-PAT-NO: 4866040
DOCUMENT-IDENTIFIER: US 4866040 A

TITLE: Aminocarnitine directed pharmaceutical agents

DATE-ISSUED: September 12, 1989

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Stracher; Alfred	Roslyn Estates	NY	11576	
Kesner; Leo	Brooklyn	NY	11234	

US-CL-CURRENT: 514/17; 424/450, 428/402.2, 514/2, 514/305, 514/535, 514/547, 514/556, 514/78, 514/821, 530/330, 930/10, 930/250, 930/30

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 9. Document ID: NZ 528874 A, WO 200061543 A2, AU 200043123 A, BR 200009765 A, NO 200104985 A, SK 200101431 A3, CZ 200103617 A3, EP 1183228 A2, IT 1306129 B, KR 2001113794 A, HU 200201446 A2, CN 1359370 A, ZA 200109291 A, JP 2002541238 W, MX 2001010359 A1, NZ 515270 A, EP 1426044 A1, EP 1435232 A1, US 20040186175 A1, US 6797281 B1, AU 776301 B2, EP 1183228 B1, AU 2004224958 A1, DE 60017388 E, US 20050079209 A1, ES 2234591 T3

L2: Entry 9 of 9 File: DWPI Sep 30, 2005

DERWENT-ACC-NO: 2000-679451
DERWENT-WEEK: 200566

TITLE: New esters of L-carnitine and alkanoyl L-carnitine compounds useful for forming liposomes for delivery of pharmacological or cosmetic agents

INVENTOR: CRITELLI, L; PISANO, C ; SALVATORI, G ; SANTANIELLO, M ; TINTI, M O

PRIORITY-DATA: 1999IT-RM00220 (April 13, 1999), 2004AU-0224958 (October 29, 2004)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
NZ 528874 A	September 30, 2005		000	A61K007/00
WO 200061543 A2	October 19, 2000	E	086	C07C229/22
AU 200043123 A	November 14, 2000		000	C07C229/22
BR 200009765 A	January 2, 2002		000	C07C229/22
NO 200104985 A	October 12, 2001		000	C07C000/00
SK 200101431 A3	February 5, 2002		000	C07C229/22
CZ 200103617 A3	February 13, 2002		000	C07C229/22
EP 1183228 A2	March 6, 2002	E	000	C07C229/22
IT 1306129 B	May 30, 2001		000	A61K000/00
KR 2001113794 A	December 28, 2001		000	C07C229/02
HU 200201446 A2	August 28, 2002		000	C07C229/22
CN 1359370 A	July 17, 2002		000	C07C229/22
ZA 200109291 A	October 30, 2002		105	C07C000/00
JP 2002541238 W	December 3, 2002		068	C07C229/22
MX 2001010359 A1	June 1, 2002		000	A61K007/00
NZ 515270 A	February 27, 2004		000	C07C229/22
EP 1426044 A1	June 9, 2004	E	000	A61K009/127
EP 1435232 A1	July 7, 2004	E	000	A61K009/127
US 20040186175 A1	September 23, 2004		000	A61K031/225
US 6797281 B1	September 28, 2004		000	A61K009/127
AU 776301 B2	September 2, 2004		000	C07C229/22
EP 1183228 B1	January 12, 2005	E	000	C07C229/22
AU 2004224958 A1	November 25, 2004		000	C07C229/22
DE 60017388 E	February 17, 2005		000	C07C229/22
US 20050079209 A1	April 14, 2005		000	A61K009/127
ES 2234591 T3	July 1, 2005		000	C07C229/22

2001010359 A1 , NZ 515270 A , EP 1426044 A1 INT-CL (IPC): A61 K 0/00; A61 K 7/00; A61 K 7/48; A61 K 9/127; A61 K 31/225; A61 K 31/337; A61 K 31/4745; A61 K 39/00; A61 K 45/00; A61 K 47/18; A61 K 47/24; A61 K 47/44; A61 K 48/00; A61 P 35/00; C07 C 0/00; C07 C 229/02; C07 C 229/22; C12 N 15/79

Terms	Documents
(ester adj5 $carnitine) same liposome	9

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Search Results - Record(s) 1 through 4 of 4 returned.

☐ 1. Document ID: US 6476243 B1

Using default format because multiple data bases are involved.

L3: Entry 1 of 4 File: USPT Nov 5, 2002

US-PAT-NO: 6476243
DOCUMENT-IDENTIFIER: US 6476243 B1

TITLE: Perfluorinated esters of alkanoyl L-carnitine for the preparation of cationic lipids for the intracellular delivery of pharmacologically active compounds

DATE-ISSUED: November 5, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Santaniello; Mose	Nettuno			IT
Critelli; Lucia	Pomezia			IT
Scafetta; Nazareno	Pavona di Albano			IT
Cima; Maria Grazia	Civitavecchia			IT
Tinti; Maria Ornella	Roma			IT
Pisano; Claudio	Aprilia			IT
Pucci; Andrea	Albano Laziale			IT

US-CL-CURRENT: 554/121; 554/123, 554/225, 554/231, 560/170, 560/172

Full | Title | Citation | Front | Review | Classification | Date | Reference | [illegible] | Claims | KWIC | Draw D

☐ 2. Document ID: US 6180355 B1

L3: Entry 2 of 4 File: USPT Jan 30, 2001

US-PAT-NO: 6180355
DOCUMENT-IDENTIFIER: US 6180355 B1
** See image for Certificate of Correction **

TITLE: Method for diagnosing and treating chronic pelvic pain syndrome

DATE-ISSUED: January 30, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY

Alexander; Richard B.	Ellicott City	MD
Ponniah; Sathibalan	Ellicott City	MD

US-CL-CURRENT: 435/7.1; 435/7.8

☐ 3. Document ID: NZ 528874 A, WO 200061543 A2, AU 200043123 A, BR 200009765 A, NO 200104985 A, SK 200101431 A3, CZ 200103617 A3, EP 1183228 A2, IT 1306129 B, KR 2001113794 A, HU 200201446 A2, CN 1359370 A, ZA 200109291 A, JP 2002541238 W, MX 2001010359 A1, NZ 515270 A, EP 1426044 A1, EP 1435232 A1, US 20040186175 A1, US 6797281 B1, AU 776301 B2, EP 1183228 B1, AU 2004224958 A1, DE 60017388 E, US 20050079209 A1, ES 2234591 T3

L3: Entry 3 of 4 File: DWPI Sep 30, 2005

DERWENT-ACC-NO: 2000-679451
DERWENT-WEEK: 200566

TITLE: New esters of L-carnitine and alkanoyl L-carnitine compounds useful for forming liposomes for delivery of pharmacological or cosmetic agents

INVENTOR: CRITELLI, L; PISANO, C ; SALVATORI, G ; SANTANIELLO, M ; TINTI, M O

PRIORITY-DATA: 1999IT-RM00220 (April 13, 1999), 2004AU-0224958 (October 29, 2004)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
NZ 528874 A	September 30, 2005		000	A61K007/00
WO 200061543 A2	October 19, 2000	E	086	C07C229/22
AU 200043123 A	November 14, 2000		000	C07C229/22
BR 200009765 A	January 2, 2002		000	C07C229/22
NO 200104985 A	October 12, 2001		000	C07C000/00
SK 200101431 A3	February 5, 2002		000	C07C229/22
CZ 200103617 A3	February 13, 2002		000	C07C229/22
EP 1183228 A2	March 6, 2002	E	000	C07C229/22
IT 1306129 B	May 30, 2001		000	A61K000/00
KR 2001113794 A	December 28, 2001		000	C07C229/02
HU 200201446 A2	August 28, 2002		000	C07C229/22
CN 1359370 A	July 17, 2002		000	C07C229/22
ZA 200109291 A	October 30, 2002		105	C07C000/00
JP 2002541238 W	December 3, 2002		068	C07C229/22
MX 2001010359 A1	June 1, 2002		000	A61K007/00
NZ 515270 A	February 27, 2004		000	C07C229/22
EP 1426044 A1	June 9, 2004	E	000	A61K009/127
EP 1435232 A1	July 7, 2004	E	000	A61K009/127
US 20040186175 A1	September 23, 2004		000	A61K031/225
US 6797281 B1	September 28, 2004		000	A61K009/127
AU 776301 B2	September 2, 2004		000	C07C229/22

EP 1183228 B1	January 12, 2005	E	000	C07C229/22
AU 2004224958 A1	November 25, 2004		000	C07C229/22
DE 60017388 E	February 17, 2005		000	C07C229/22
US 20050079209 A1	April 14, 2005		000	A61K009/127
ES 2234591 T3	July 1, 2005		000	C07C229/22

2001010359 A1 , NZ 515270 A , EP 1426044 A1 INT-CL (IPC): A61 K 0/00; A61 K 7/00; A61 K 7/48; A61 K 9/127; A61 K 31/225; A61 K 31/337; A61 K 31/4745; A61 K 39/00; A61 K 45/00; A61 K 47/18; A61 K 47/24; A61 K 47/44; A61 K 48/00; A61 P 35/00; C07 C 0/00; C07 C 229/02; C07 C 229/22; C12 N 15/79

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 4. Document ID: DE 69918974 T2, WO 9957094 A2, AU 9938465 A, EP 1075461 A2, KR 2001043234 A, IT 1299172 B, JP 2002513779 W, US 6476243 B1, EP 1075461 B1, DE 69918974 E, ES 2226384 T3

L3: Entry 4 of 4 File: DWPI Aug 11, 2005

DERWENT-ACC-NO: 2000-023538
DERWENT-WEEK: 200553
COPYRIGHT 2005 DERWENT INFORMATION LTD
TITLE: New perfluorinated alkanoyl-L-carnitine esters useful for production of liposomes

INVENTOR: CIMA, G; CRITELLI, L ; PISANO, C ; PUCCI, A ; SANTANIELLO, M ; SCAFETTA, N ; TINTI, O ; CIMA, M G ; TINTI, M O

PRIORITY-DATA: 1998IT-RM00293 (May 6, 1998)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
DE 69918974 T2	August 11, 2005		000	C07C229/22
WO 9957094 A2	November 11, 1999	E	021	C07C229/22
AU 9938465 A	November 23, 1999		000	
EP 1075461 A2	February 14, 2001	E	000	C07C229/22
KR 2001043234 A	May 25, 2001		000	C07C229/22
IT 1299172 B	February 29, 2000		000	C07C000/00
JP 2002513779 W	May 14, 2002		021	C07C229/22
US 6476243 B1	November 5, 2002		000	C07F003/06
EP 1075461 B1	July 28, 2004	E	000	C07C229/22
DE 69918974 E	September 2, 2004		000	C07C229/22
ES 2226384 T3	March 16, 2005		000	C07C229/22

INT-CL (IPC): A61 K 9/127; A61 K 47/48; C07 C 0/00; C07 C 229/22; C07 F 3/06

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

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Terms	Documents
(alkanoyl adj5 $carnitine) same liposome	4

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L2: Entry 1 of 9 File: USPT Sep 28, 2004

DOCUMENT-IDENTIFIER: US 6797281 B1
** See image for Certificate of Correction **
TITLE: Esters of I-carnitine or alkanoyl I-carnitines

Detailed Description Text (32):
According to the present invention, the compounds of formula (II) are esters of L-carnitine, useful for the preparation of liposomes which possess potent activity in drug delivery and present characteristics of stability and selectivity in reaching the target organ comparable to those of the compounds of formula (I) described above. The same advantageous properties are applicable in case of cosmetics.

Detailed Description Text (55):
According to the present invention, the compounds of formula (III) are esters of L-carnitine, useful for the preparation of liposomes which possess potent activity in promoting drug delivery and present characteristics of stability and selectivity in reaching the target organ comparable to those of the compounds of formula (I) described above.

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L2: Entry 5 of 9 File: USPT Oct 26, 1999

DOCUMENT-IDENTIFIER: US 5972600 A
TITLE: Separation of active complexes

CLAIMS:

17. The product of claim 12, wherein the liposome is selected from the group consisting of phosphatidylethanolamine [PE], phosphatidyl choline [PC], dioleyloxy phosphatidylethanolamine [DOPE], n-[1-(2,3-dioleyloxy) propyl]-N,N,N-trimethylammonium chloride [DOTMA], dioleoylphosphatidylcholine [DOPC], 2,3-dioleyloxy-N-[2-(sperminecarboxyamido)ethyl]-N,N-dimethyl-1-propanamin ium trifluoroacetate [DOSPA], [DOTAP], [DOGG], spermine-5-carboxyglycine(N'-stearyl-N'-stearyl)amide tetra-trifluoroacetic acid salt [DOGS], 1,2 dimyristyloxypropyl-3-dimehtyl-hydroxyethyl ammonium bromide [DMRIE], 1,2 dimyristoyl-sn-glycero-3-ethylphosphocholine [EDMPC], 1,2 dioleoyl-sn-glycero-3-ethylphosphocholine [EDOPC], 1 palmitoyl, 2 myristoyl-sn-glycero-3-ethylphosphocholine [EPMPC], dimethyldioctadecylammonium bromide [DDAB], cetyldimethylethylammonium bromide [CDAB], cetyltrimethylethylammonium bromide [CTAB],], monooleoyl-glycerol [MOG], cholesterol [Chol], cationic bile salts, spermine-5-carboxyglycine (N'-stearyl-N'-oleyl) amide tetratrifluoroacetic acid salt [JK-75], spermine-5-carboxyglycine (N'-stearyl- N'-elaidyl) amide tetratrifluoroacetic acid salt [JK-76], agmatinyl carboxycholesterol acetic acid salt [AG-Chol], spermine-5-carboxy-.beta.-alanine cholesteryl ester tetratrifluoroacetic acid salt [CAS], 2,6-diaminohexanoeyl .beta.-alanine cholesteryl ester bistrifluoroacetic acid salt [CAL], 2,4-diaminobutyroyl .beta.-alanine cholesteryl ester bistrifluoroacetic acid salt [CAB], N,N-bis (3-aminopropyl)-3-aminopropionyl .beta.-alanine cholesteryl ester tristrifluoroacetic acid salt [CASD], [N,N-bis(2-hydroxyethyl)-2-aminoethyl] aminocarboxy cholesteryl ester [JK-154], carnitine ester lipids, stearyl carnitine ester, myristyl carnitine ester, stearyl stearoyl carnitine ester chloride salt [SSCE], L-stearyl stearoyl carnitine ester [L-SSCE], stearyl oleoyl carnitine ester chloride [SOCE], palmityl palmitoyl carnitine ester chloride [PPCE], myristyl myristoyl carnitine ester chloride [MMCE], L-myristyl myristoyl carnitine ester chloride [L-MMCE].

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Search Results -

Terms	Documents
carnitine adj10 liposome	9

Database:
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US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L1

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Search History

DATE: Monday, December 19, 2005 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L1	carnitine adj10 liposome	9	L1

END OF SEARCH HISTORY

L1: Entry 3 of 9 File: USPT Mar 2, 1999

DOCUMENT-IDENTIFIER: US 5876747 A
TITLE: Liposome preferentially traveling to cardiac and skeletal muscles

Abstract Text (1):
Carnitine, aminocarnitine and cysteic acid serve as carriers to bring pharmaceutically active compounds to desired sites in the body, e.g. skeletal muscle or the heart. The pharmaceutically active compound can be a protease inhibitor, a cardioactive drug for combating arrythmia, etc. The linkage is chemical through one or more alcohol, carboxyl or amine groups using reagents such as glutaraldehyde, dicarboxylic acid anhydrides and acid halides and carbodiimides. Carnitine derivatives are also incorporated into liposomes which are then used as carriers of active pharmaceutical agents.

Brief Summary Text (41):
In accordance with another aspect of the invention, the carrier which brings the active material to the predetermined site, e.g. carnitine for muscle, can be chemically linked to a phosphatide in the form of a liposome. The pharmaceutically active compound then exists enclosed as an aqueous solution inside the liposome. The chemical linkage between carrier and phosphatic can be direct or indirect, e.g. through a linking agent coupled to the phosphatide and to carnitine, aminocarnitine or cysteic acid.

Brief Summary Text (42):
Carnitine can be incorporated into liposomes in a number of ways and still retain the carbonyl and trimethylamine functional groups needed for the recognition of the carnitine receptor site. One way to do this is to use phosphatidylcarnitine or a mixture of phospholipids and lipids containing some fraction of its components as phosphatidylcarnitine. Phosphatidylcarnitine is synthesized from phosphatidic acid of desired fatty acid composition, optical activity and any other characteristics required. This is then reacted with the phthalimidomethyl ester of carnitine using triisopropylbenzenesulfonyl chloride in pyridine as the condensing agent. The ester protecting group is then removed using sodium thiophenoxide as hydrolyzing agent to yield phosphatidylcarnitine (XXXIV).

Brief Summary Text (45):
Carnitine can also be added to liposomes by covalent linkage of carnitine to phospholipids with available functional groups. Then these derivatized phospholipids can be made into liposomes directly or mixed with other phospholipids and then made into liposomes.

Brief Summary Text (51):
In the past, a major drawback to the use of liposomes as vectors for drug delivery has been the fact that when injected into the blood stream they are taken up predominantly by the liver and reticuloendothelial system so that drugs active in disease conditions affecting other organs cannot be delivered efficiently by this procedure. In addition, liposomes cannot be administered orally because pancreatic lipase enzymes in the intestine break down the liposomes during digestion. The present invention offers a means of eliminating both of these drawbacks. Because of the presence of carnitine or aminocarnitine as part of the liposomal structure, the drug-containing liposomes will be delivered in much greater amounts to the desired

target organs and much less will be metabolized by the liver. In addition, the presence of phosphatidyl carnitine in the liposome structure will present the intestinal lipase enzymes with a novel chemical structure that is apt to be far more resistant to digestion than naturally occurring lipids. This also holds true for liposomes containing amino carnitine and would serve to facilitate oral administration of organ specific pharmacologically active agents.

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L1: Entry 4 of 9 File: USPT Apr 16, 1991

DOCUMENT-IDENTIFIER: US 5008288 A
TITLE: Carnitine directed pharmaceutical agents

Abstract Text (1):
Carnitine, aminocarnitine and cysteic acid serve as carriers to bring pharmaceutically active compounds to desired sites in the body, e.g. skeletal muscle or the heart. The pharmaceutically active compound can be a protease inhibitor, a cardioactive drug for combating arrythmia, etc. The linkage is chemical through one or more alcohol, carboxyl or amine groups using reagents such as glutaraldehyde, dicarboxylic acid anhydrides and acid halides and carbodiimides. Carnitine derivatives are also incorporated into liposomes which are then used as carriers of active pharmaceutical agents.

Brief Summary Text (40):
In accordance with another aspect of the invention, the carrier which brings the active material to the predetermined site, e.g. carnitine for muscle, can be chemically linked to a phosphatide in the form of a liposome. The pharmaceutically active compound then exists enclosed as an aqueous solution inside the liposome. The chemical linkage between carrier and phosphatic can be direct or indirect, e.g. through a linking agent coupled to the phosphatide and to carnitine, aminocarnitine or cysteic acid.

Brief Summary Text (41):
Carnitine can be incorporated into liposomes in a number of ways and still retain the carbonyl and trimethylamine functional groups needed for the recognition of the carnitine receptor site. One way to do this is to use phosphatidylcarnitine or a mixture of phospholipids and lipids containing some fraction of its components as phosphatidylcarnitine. Phosphatidylcarnitine is synthesized from phosphatidic acid to desired fatty acid composition, optical activity and any other characteristics required. This is then reacted with the phthalimidomethyl ester of carnitine using triisopropylbenzenesulfonyl chloride in pyridine as the condensing agent. The ester protecting group is then removed using sodium thiophenoxide as hydrolyzing agent to yield phosphatidylcarnitine (XXXIV).

Brief Summary Text (44):
Carnitine can also be added to liposomes by covalent linkage of carnitine to phospholipids with available functional groups. Then these derivatives phospholipids can be made into liposomes directly or mixed with other phospholipids and then made into liposomes.

Brief Summary Text (50):
In the past, a major drawback to the use of liposomes as vectors for drugs delivery has been the fact that when injected into the blood stream they are taken up predominantly by the liver and reticuloendothelial system so that drugs active in disease conditions affecting other organs cannot be delivered efficiently by this procedure. In addition, liposomes cannot be administered orally because pancreatic lipase enzymes in the intestine break down the liposomes during digestion. The present invention offers a means of eliminating both of these drawbacks. Because of the presence of carnitine or aminocarnitine as part of the liposomal structure, the drug-containing liposomes will be delivered in much greater amounts to the desired

target organs and much less will be metabolized by the liver. In addition, the presence of phosphatidyl carnitine in the liposome structure will present the intestinal lipase enzymes with a novel chemical structure that is apt to be far more resistant to digestion than naturally occurring lipids. This also holds true for liposomes containing amino carnitine and would serve to facilitate oral administration of organ specific pharmacologically active agents.

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☐ 1. Document ID: US 6797281 B1

Using default format because multiple data bases are involved.

L1: Entry 1 of 9 File: USPT Sep 28, 2004

US-PAT-NO: 6797281
DOCUMENT-IDENTIFIER: US 6797281 B1
** See image for Certificate of Correction **

TITLE: Esters of I-carnitine or alkanoyl I-carnitines

DATE-ISSUED: September 28, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Pisano; Claudio	Aprilia			IT
Tinti; Maria Ornella	Rome			IT
Santaniello; Mose	Nettuno			IT
Critelli; Luciana	Pomezia			IT
Salvatori; Giovanni	Rome			IT

US-CL-CURRENT: 424/450; 424/43, 424/434, 424/449, 424/46, 514/506, 554/30

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 2. Document ID: US 6476243 B1

L1: Entry 2 of 9 File: USPT Nov 5, 2002

US-PAT-NO: 6476243
DOCUMENT-IDENTIFIER: US 6476243 B1

TITLE: Perfluorinated esters of alkanoyl L-carnitine for the preparation of cationic lipids for the intracellular delivery of pharmacologically active compounds

DATE-ISSUED: November 5, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Santaniello; Mose	Nettuno			IT
Critelli; Lucia	Pomezia			IT

Scafetta; Nazareno	Pavona di Albano	IT
Cima; Maria Grazia	Civitavecchia	IT
Tinti; Maria Ornella	Roma	IT
Pisano; Claudio	Aprilia	IT
Pucci; Andrea	Albano Laziale	IT

US-CL-CURRENT: 554/121; 554/123, 554/225, 554/231, 560/170, 560/172

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 3. Document ID: US 5876747 A

L1: Entry 3 of 9 File: USPT Mar 2, 1999

US-PAT-NO: 5876747
DOCUMENT-IDENTIFIER: US 5876747 A

TITLE: Liposome preferentially traveling to cardiac and skeletal muscles

DATE-ISSUED: March 2, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Stracher; Alfred	Roslyn Estates	NY	11576	
Kesner; Leo	Brooklyn	NY	11234	

US-CL-CURRENT: 424/450; 514/78, 514/821, 554/79, 554/80

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 4. Document ID: US 5008288 A

L1: Entry 4 of 9 File: USPT Apr 16, 1991

US-PAT-NO: 5008288
DOCUMENT-IDENTIFIER: US 5008288 A

TITLE: Carnitine directed pharmaceutical agents

DATE-ISSUED: April 16, 1991

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Stracher; Alfred	Roslyn Estates	NY	11576	
Kesner; Leo	Brooklyn	NY	11234	

US-CL-CURRENT: 514/535; 424/450, 428/402.2, 514/17, 514/2, 514/305, 514/547, 514/556, 514/821, 530/330, 530/812

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 5. Document ID: US 4866040 A

L1: Entry 5 of 9 File: USPT Sep 12, 1989

US-PAT-NO: 4866040
DOCUMENT-IDENTIFIER: US 4866040 A

TITLE: Aminocarnitine directed pharmaceutical agents

DATE-ISSUED: September 12, 1989

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Stracher; Alfred	Roslyn Estates	NY	11576	
Kesner; Leo	Brooklyn	NY	11234	

US-CL-CURRENT: 514/17; 424/450, 428/402.2, 514/2, 514/305, 514/535, 514/547, 514/556, 514/78, 514/821, 530/330, 930/10, 930/250, 930/30

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 6. Document ID: EP 279887 A2

L1: Entry 6 of 9 File: EPAB Aug 31, 1988

PUB-NO: EP000279887A2
DOCUMENT-IDENTIFIER: EP 279887 A2
TITLE: Carnitine directed pharmaceutical agents and their use for the manufacture of a medicament for the treatment of muscle disorder.

PUBN-DATE: August 31, 1988

INVENTOR-INFORMATION:

NAME	COUNTRY
STRACHER, ALFRED	

US-CL-CURRENT: 424/450
INT-CL (IPC): A61K 9/50; A61K 37/64; A61K 47/00; C07C 101/30; C07C 103/50; C07C 149/247; C07K 5/02
EUR-CL (EPC): A61K009/127; A61K047/48, A61K047/48 , C07C229/22 , C07C229/26 , C07C323/58 , C07K005/02 , C07K005/06

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 7. Document ID: NZ 528874 A, WO 200061543 A2, AU 200043123 A, BR 200009765 A, NO 200104985 A, SK 200101431 A3, CZ 200103617 A3, EP 1183228 A2, IT 1306129 B, KR 2001113794 A, HU 200201446 A2, CN 1359370 A, ZA 200109291 A, JP 2002541238 W, MX

2001010359 A1, NZ 515270 A, EP 1426044 A1, EP 1435232 A1, US 20040186175 A1, US 6797281 B1, AU 776301 B2, EP 1183228 B1, AU 2004224958 A1, DE 60017388 E, US 20050079209 A1, ES 2234591 T3

L1: Entry 7 of 9 File: DWPI Sep 30, 2005

DERWENT-ACC-NO: 2000-679451
DERWENT-WEEK: 200566

TITLE: New esters of L-carnitine and alkanoyl L-carnitine compounds useful for forming liposomes for delivery of pharmacological or cosmetic agents

INVENTOR: CRITELLI, L; PISANO, C ; SALVATORI, G ; SANTANIELLO, M ; TINTI, M O

PRIORITY-DATA: 1999IT-RM00220 (April 13, 1999), 2004AU-0224958 (October 29, 2004)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
NZ 528874 A	September 30, 2005		000	A61K007/00
WO 200061543 A2	October 19, 2000	E	086	C07C229/22
AU 200043123 A	November 14, 2000		000	C07C229/22
BR 200009765 A	January 2, 2002		000	C07C229/22
NO 200104985 A	October 12, 2001		000	C07C000/00
SK 200101431 A3	February 5, 2002		000	C07C229/22
CZ 200103617 A3	February 13, 2002		000	C07C229/22
EP 1183228 A2	March 6, 2002	E	000	C07C229/22
IT 1306129 B	May 30, 2001		000	A61K000/00
KR 2001113794 A	December 28, 2001		000	C07C229/02
HU 200201446 A2	August 28, 2002		000	C07C229/22
CN 1359370 A	July 17, 2002		000	C07C229/22
ZA 200109291 A	October 30, 2002		105	C07C000/00
JP 2002541238 W	December 3, 2002		068	C07C229/22
MX 2001010359 A1	June 1, 2002		000	A61K007/00
NZ 515270 A	February 27, 2004		000	C07C229/22
EP 1426044 A1	June 9, 2004	E	000	A61K009/127
EP 1435232 A1	July 7, 2004	E	000	A61K009/127
US 20040186175 A1	September 23, 2004		000	A61K031/225
US 6797281 B1	September 28, 2004		000	A61K009/127
AU 776301 B2	September 2, 2004		000	C07C229/22
EP 1183228 B1	January 12, 2005	E	000	C07C229/22
AU 2004224958 A1	November 25, 2004		000	C07C229/22
DE 60017388 E	February 17, 2005		000	C07C229/22
US 20050079209 A1	April 14, 2005		000	A61K009/127
ES 2234591 T3	July 1, 2005		000	C07C229/22

2001010359 A1 , NZ 515270 A , EP 1426044 A1 INT-CL (IPC): A61 K 0/00; A61 K 7/00; A61 K 7/48; A61 K 9/127; A61 K 31/225; A61 K 31/337; A61 K 31/4745; A61 K 39/00; A61 K 45/00; A61 K 47/18; A61 K 47/24; A61 K 47/44; A61 K 48/00; A61 P 35/00; C07 C 0/00; C07 C 229/02; C07 C 229/22; C12 N 15/79

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 8. Document ID: DE 69918974 T2, WO 9957094 A2, AU 9938465 A, EP 1075461 A2, KR 2001043234 A, IT 1299172 B, JP 2002513779 W, US 6476243 B1, EP 1075461 B1, DE 69918974 E, ES 2226384 T3

L1: Entry 8 of 9 File: DWPI Aug 11, 2005

DERWENT-ACC-NO: 2000-023538
DERWENT-WEEK: 200553
COPYRIGHT 2005 DERWENT INFORMATION LTD
TITLE: New perfluorinated alkanoyl-L-carnitine esters useful for production of liposomes

INVENTOR: CIMA, G; CRITELLI, L ; PISANO, C ; PUCCI, A ; SANTANIELLO, M ; SCAFETTA, N ; TINTI, O ; CIMA, M G ; TINTI, M O

PRIORITY-DATA: 1998IT-RM00293 (May 6, 1998)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
DE 69918974 T2	August 11, 2005		000	C07C229/22
WO 9957094 A2	November 11, 1999	E	021	C07C229/22
AU 9938465 A	November 23, 1999		000	
EP 1075461 A2	February 14, 2001	E	000	C07C229/22
KR 2001043234 A	May 25, 2001		000	C07C229/22
IT 1299172 B	February 29, 2000		000	C07C000/00
JP 2002513779 W	May 14, 2002		021	C07C229/22
US 6476243 B1	November 5, 2002		000	C07F003/06
EP 1075461 B1	July 28, 2004	E	000	C07C229/22
DE 69918974 E	September 2, 2004		000	C07C229/22
ES 2226384 T3	March 16, 2005		000	C07C229/22

INT-CL (IPC): A61 K 9/127; A61 K 47/48; C07 C 0/00; C07 C 229/22; C07 F 3/06

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 9. Document ID: EP 279887 A, US 5876747 A, JP 63174936 A, EP 279887 B1, DE 3751036 G

L1: Entry 9 of 9 File: DWPI Aug 31, 1988

DERWENT-ACC-NO: 1988-243463
DERWENT-WEEK: 199916
COPYRIGHT 2005 DERWENT INFORMATION LTD
TITLE: Carnitine, amino:carnitine or cysteic acid - used as carrier for pharmaceutically active cpd. or in liposome(s) to direct to cardiac and skeletal muscle

INVENTOR: KESNER, L; STRACHER, A

PRIORITY-DATA: 1987US-0003888 (January 15, 1987), 1986US-0816546 (January 6, 1986), 1989US-0347361 (May 4, 1989), 1991US-0638948 (January 9, 1991), 1992US-0912068 (July 8, 1992)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 279887 A	August 31, 1988	F	027	
US 5876747 A	March 2, 1999		000	A61K009/127
JP 63174936 A	July 19, 1988		000	
EP 279887 B1	February 1, 1995	E	021	C07C229/22
DE 3751036 G	March 16, 1995		000	C07C229/22

INT-CL (IPC): A61K 9/10; A61K 9/127; A61K 9/50; A61K 31/685; A61K 37/64; A61K 38/55; A61K 47/00; A61K 47/06; C07C 101/30 ; C07C 103/50; C07C 149/24; C07C 229/22; C07C 237/08; C07C 309/18; C07K 5/02

Terms	Documents
carnitine adj10 liposome	9

L3: Entry 14 of 14 File: USPT Sep 3, 1996

DOCUMENT-IDENTIFIER: US 5552156 A
TITLE: Liposomal and micellular stabilization of camptothecin drugs

Brief Summary Text (8):
This invention overcomes both the insolubility problems and instability problems of the camptothecin drugs administered in their free form. It has been discovered that the lactone ring of the camptothecin drugs is stabilized in the membranes of vesicles. The present invention provides water soluble, stable, highly pharmacologically active camptothecin drugs by stabilizing the camptothecin drugs in vesicles such as liposomes and micelles. Typically, the camptothecin drugs bind the lipid bilayer membrane of the liposome and the surfactant monolayer membrane of the micelles with high affinity. The liposome-bound drug is protected from hydrolysis, thus preserving the antitumor activity of the drug. The liposome is comprised of lipids such as, for example phospholipids or cholesterol. For the camptothecin drugs which have a lower affinity for the liposome membrane and thus disassociate from the liposomal membrane to reside in the interior of liposome, the pH of the internal environment of the liposomes is reduced thereby preventing hydrolysis of such camptothecin drugs. Camptothecin drugs are also stabilized by association with micelles comprised of surfactants such as sodium dodecylsulfate (SDS), octylphenolpolyoxyethylene glycol and sorbitan mono-oleate.

Detailed Description Text (2):
The present invention provides water soluble, stable, highly pharmacologically active camptothecin drugs by solubilizing the camptothecin drugs in receptacles. The receptacles are liposomes, comprised of lipids such as cholesterol, or phospholipids, or micelles comprised of surfactant such as, for example, sodium dodecylsulfate, octylphenolpolyoxyethylene glycol, or sorbitan mono-oleate. Typically, the camptothecin drugs bind the lipid bilayer the membrane of liposome with high affinity. The liposome bound camptothecin drug intercalates between the acyl chains of the lipid. The lactone ring of the camptothecin membrane-bound drug is thereby removed from the aqueous environment inside and outside of the liposome and thus protected from hydrolysis. Since the liposome-bound drug is protected from hydrolysis, the antitumor activity of the drug is preserved. For the camptothecin drugs, such as topotecan, which have a lower affinity for the liposome membrane and thus disassociate from the liposome membrane to reside in the interior of liposome, the pH of the interior of the liposomes may be reduced thereby preventing hydrolysis of such camptothecin drugs.

Detailed Description Text (5):
As used herein the terms "camptothecin drugs are associated with liposomes" means either that some or all of the camptothecin drug is located in one or more of the compartments of the liposome or the camptothecin drug is bound to the membrane of the liposome, to provide a liposome comprising a lipid bilayer membrane and a camptothecin drug. As used herein, the phrase "bound to lipid membrane" means that at least the lactone ring of some or all of the camptothecin drug binds to the lipid membrane of the liposome where the liposome contains more than 1 bilayer membrane the camptothecin drug is bound to at least 1 membrane. Those camptothecin drugs that have a high affinity for such membrane tend to remain bound to the

membrane. Those camptothecin drugs with a low affinity for the liposome membrane, such as topotecan, will at least partially disassociate from the liposome membrane and reside in the liposome compartment.

Detailed Description Text (9):
The liposomes and micelles containing camptothecin drugs are administered to the cancer patient, typically intravenously. The liposomes and micelles are carried by the circulatory system to the cancer cells where the membrane of the vesicle fuses to the membrane of the cancer cell thereby releasing the camptothecin drug to the cancer cell, or where the liposomes and micelles remain adjacent to the cancer cells and the camptothecin drugs diffuses from the liposomes and micelles to be taken up by the cancer cells.

Detailed Description Text (18):
DSPC, since it is solid phase at 37.degree. C., (the average temperature of humans), limits the diffusion of the camptothecin drug from the liposome and thus can be employed to time release the camptothecin drugs.

Detailed Description Text (51):
The camptothecin drugs are intrinsically intensely fluorescent. Fluorescence is associated with the extended conjugation of the quinoline ring system. The liposomes of Examples 1-7 were characterized for the presence of the camptothecin drugs, using excitation and emission spectrography, and fluorescence anisotropy.

Detailed Description Text (56):
FIG. 1A shows the excitation and emission spectra of camptothecin free in solution and camptothecin that is bound to liposomes composed of (DMPG) and to DMPC. The relative fluorescence intensity of 1.times.10.sup.-6 M of camptothecin free in PBS buffer at 37.degree. C. is shown. The emission spectra of the camptothecin was recorded using exciting light of 370 nm. Where camptothecin binds to DMPG liposomes, the emission intensity decreases and the .lambda..sub.max of the camptothecin emission spectrum exhibits a shift to a lower wavelength, that is "blue shifts," about 16 nm relative to the emission spectra of free camptothecin. The shift in the emission spectrum demonstrates that the camptothecin drug binds to and is solubilized in the membrane of the liposome. Specifically, this shift indicates that the camptothecin chromophore penetrates into the acyl chain region of the liposome membrane. As shown in FIG. 1A, a spectral shift of about 5 nm was observed for camptothecin associated with DMPC liposomes, indicating the camptothecin drug was soluble in the DMPC liposome membrane, as well.

Detailed Description Text (65):
Thus, the spectral changes of the various camptothecin drugs establish that when associated with the liposomes, the camptothecin drugs bind to the lipid membrane of the liposome.

Detailed Description Text (88):
Thus, among the camptothecin drugs studied, the CMC has the highest binding affinity for each type of liposome, the 10,11-methylenedioxycamptothecin and camptothecin have intermediate binding affinities, while topotecan exhibits the lowest binding affinity for liposomes.

Detailed Description Text (97):
FIGS. 7A, 7B and 7C also show the stability profiles of CMC, camptothecin, and topotecan in the presence of DMPC and DMPG liposomes having lipid concentrations of 0.29M. In samples containing DMPC liposomes, the bound drug levels for CMC, camptothecin, and topotecan were estimated 99%, 97%, and 74% respectively; while bound drug levels in samples containing DMPG liposomes were 99%, 97%, and 93%, respectively.

Detailed Description Text (101):

Additional evidence that the fluorochrome of the camptothecin drugs penetrates into the membrane of the liposome comes from iodide quenching data. Iodide has an immeasurably small permeation of the liposome membrane and is able to discriminate between camptothecin drug molecules free in solution and those molecules located in the interior of the liposome membrane. These methods have been described in detail in Burke and Tritton, Biochemistry (1985) 24: 5972-5980; G. L. Jendrasiak, Chem. Phys. Lipids 9: 133-146 (1992); and, M. Cranney et al. Biochem. Biophys. ACTA 735, 418-425, which are incorporated herein by reference. The quenching studies were conducted using 0.5M iodide in PBS buffer.

Detailed Description Text (102):
The quenching of fluorescence of both camptothecin free in PBS and liposome membrane bound camptothecin by iodide ions was conducted at a constant halide concentration of 0.5M, in the presence of 2 mM sodium thiosulfate to prevent the oxidation of iodide. The camptothecin concentration was 1.times.10.sup.-6 M and the iodide concentration was varied from 0 to 0.5M, and the chloride concentration was adjusted accordingly. The quenching experiments for the camptothecin bound to DMPC or DMPG liposome membranes were done at a lipid concentration of 100 mg/mL, so that the fraction of the bound camptothecin was more than 97%.

Detailed Description Text (103):
Results of the iodide quenching experiments are shown in FIG. 8. Fluorescence of camptothecin free in PBS having a pH of 7.4 is quenched significantly by 0.5M iodide, F.sub.0 /F being about 54.3. Fluorescence of the liposome membrane bound camptothecin is quenched to relatively lower extent, for instance, F.sub.0 /F, for camptothecin bound to DMPC liposomes is only 4.1 (see Plot C). Also, there is a clear cut upward curvature in the F.sub.0 /F vs. [I] plot (curve "A", FIG. 5) for camptothecin free in PBS whereas F.sub.0 /F vs. [I] plot for camptothecin bound with DMPC membranes is linear. Quenching of fluorescence is believed to proceed via the dynamic (or collisional) and static quenching processes. Fluorescence quenching by a quencher molecule in contact with the fluorophore at the instant of excitation is considered to be static quenching. The static and dynamic quenching processes are separated by the following modified form of the Stern-Volmer equation (Eftink & Ghiron, 1976):

Detailed Description Text (104):
where, V is the static quenching constant and K.sub.sv the dynamic or collisional quenching constant. The V and K.sub.sv values were obtained by fitting the quenching data to equation 3 with a value of V which gave the best correlation coefficient for the plot of F.sub.0 /Fe.sup.v[Q] vs. [Q]. The upward curvature of the quenching data of free camptothecin free in PBS seen in FIG. 8 could be attributed to the static quenching process. The straight line "B", which is tangential to the F.sub.0 /F vs. [I] plot for free camptothecin in PBS, represents the dynamic part of the iodide quenching of camptothecin fluorescence, the slope of which is equal to K.sub.sv (slope=44 3M.sup.-1 where V=14M.sup.-1 correlation coefficient=0.9993). The Stern-Volmer plot for the liposome bound camptothecin is linear, curve "C", FIG. 8, the slope being 6.1M.sup.-1. It is evident that DMPC liposome bound camptothecin does not involve any significant static quenching process, probably due to the location of the fluorophore well inside the liposome membrane. The dashed line represents the static and dynamic quenching components camptothecin free in solution is determined by F.sub.0 /F values.

Detailed Description Text (108):
Thus for camptothecin drugs which have a low binding affinity or even an intermediate binding affinity for liposome or micelle membranes, such as CMC, camptothecin, topotecan, and 9-aminocamptothecin, these drugs can be further stabilized by lowering the pH of the compartment of the liposome or micelle.

Detailed Description Text (109):
The fact that liposome-associated camptothecin drugs are stable indicate that the

lactone ring of the camptothecin drugs penetrates into the liposome membrane. The 10,11-methylenedioxycamptothecin, and 9-chloro-10,11-methylenedioxycamptothecin are preferred for use with liposomes of because of their lipophilicity and thus improved binding to lipid membranes. It is preferred that the 10,11-methylenedioxycamptothecin, and 9-chloro-10,11-methylenedioxycamptothecin be associated with either DMPG liposomes, or DSPC liposomes having a pH of less than 6. Generally, the DMPG is preferred over the DMPC. Thus camptothecin drugs are stabilized in liposomes either by binding the liposome membrane or by locating in the compartment where the pH is lower than 6, preferably 5 or below.

Detailed Description Text (114):
Thus liposomes and micelles composed of camptothecin drugs are an effective means of conserving the intact, active forms of the drugs; clinical use of such liposomes and micelles will aid in controlling the proliferation of tumorous tissue in patients undergoing chemotherapy.

Current US Original Classification (1):
424/450

CLAIMS:

1. A liposome, comprising a camptothecin drug or mixtures of camptothecin drugs containing a least one lactone ring, and a bilayer membrane comprised of lipid, at least some of the said lactone ring being intercalated in the bilayer so that said ring is protected from hydrolysis at an internal liposomal compartment pH of from about 3 to about 7.4.

9. The liposome of claim 1, wherein the drug comprises camptothecin.

1. providing a liposome as a delivery vehicle comprising: a camptothecin drug or mixtures of camptothecin drugs containing a least one lactone ring, and a bilayer membrane comprised of lipid, at least some of the said lactone ring being intercalated in the bilayer so that said ring is protected from hydrolysis at an internal liposomal compartment pH of from about 3 to about 7.4;

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